July 30, 1946.

Dear Dr. Luria-

I have spent the past two weeks on a wild goose chase: finally managing to secure two double biochemical mutants in B/r (Y38-Y43 arginine;methionine and Y39-Y44 histidine;p-aminobenzoic ac.) Several experiments at attempting to get prototrophs from their interaction, and from B/r and K-12 mutants, have been entirely negative. I do not think,therefore,that you will have any particular use for them. This is a fortunate occurrence,because it connects very beautifully with the observation that you stated in your last letter that your recent experiments indicate no recombinations of virus resistance in B. It is clear then,I think, that we shall have to continue to work with K-12 strains. If you have other strains of E. coli (preferably motile-just a hunch of mine) which are susceptible to this series of viruses I might try the same with them. I am looking very hard for a possible instance of 'heterothallism.'

Thank you very much for the information on the phage susceptibility pattern of K-12. It does look like there may be a lot of material here. I would suggest that it would be important for you to ascertain whether complex resistance mutants occur in K-12; if so there is the chance of analysing them. I have gotten what I think are some recombinations of biochemical requirements and virus resistance (aside from resistant and susceptible prototrophs) but I'll have to look into that more carefully. Also, from the ratios of resistant and susceptible prototrophs in various 'crosses' there seems be be some sort of linkage (about 50 %) between resistance to T-1 and either proline- or threonineless. Since this will complicate considerably any use of biochemical factors as selectors, more work will have to be done with a vraiety of these mutants to find sets that will allow a more random distribution of resistance in the prototrophs.

I feel competent

to work with the segregation of single resistante factors, but I am very anxious for your collaboration, or rather to collaborate with you, on the complex mutation problem. (A word on terminology- I mean by complex a phenotype different in several characters obtained by a 'single mutational step' as distinguished from multiple mutations which are obtained in iterated steps+)

I expect to be in New York in about two weeks, and will endeavour to visit you, bringing the latest information, and possibly the most suitable cultures. This is not certain, however; I would appreciate it if you could let me know when you expect not to be at Cold Spring Harbour.

Very sincerely yours,

Joshua Lederberg.